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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 03/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/058,069	BRASLAWSKY ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,29,38-40,55,62,63,68,75-81 and 84-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,29,38-40,55,62,63,68,75-81 and 84-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-19, 21-28, 30-37, 41-54, 56-61, 64-67, 69-74 and 82-83 are cancelled.

Claims 20, 29, 55, 68, 80-81 and 85 have been amended.

Claims 80-92 have been added.

2. Claims 20, 29, 38-40, 55, 62-63, 68, 75-81 and 84-92 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

4. The rejection of claims 20, 29, 38-40, 55-57, 62-63, 68-70, 75-92 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "a tetravalent antibody dimer..." that "has two antigen-binding sites" is withdrawn in view of the amendments to the claims.

5. The rejection of claims 55, 68 and 81 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "wherein said antibody dimer is a chimeric antibody...". is withdrawn in view of the amendments to the claims.

6. The rejection of claims 20, 29, 38-40, 55, 57, 62-63, 68, 70, 75-81, 83-92 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims is withdrawn in view of the amendments to the claims.

7. The rejection of claims 20, 29, 38-40, 63, 76-80 and 84-92 under 35 U.S.C. 103(a) as being unpatentable over Beresford et al (International Journal of Cancer, 81(6):911-917, 11 June 1999) in view of Kashmiri et al (WO 00/26394, 5/11/00) and Anderson et al (U.S. Patent 6,348,581 B1, priority at least to 2/18,1998, cited previously) and Thorpe et al (U.S. Patent 6,342,219 B1, 4/28/1999, cited previously) is withdrawn in view of the amendments to the claims, which now recite that the CH3 domain be fused directly to the hinge region and no longer read on a tetravalent scFv dimer.

8. The rejection of claims 56, 69 and 82 under 35 U.S.C. 103(a) as being unpatentable over Gillies et al (Human Antibodies and Hybridomas, 1(1):47-54, 1990, cited previously) as evidenced by the specification in view of Kashmiri et al (WO 00/26394, 5/11/00) and Anderson et al (U.S. Patent 6,348,581 B1, priority at least to 2/18/1998, cited previously) and Thorpe et al (U.S. Patent 6,342,219 B1, 4/28/1999, cited previously) is withdrawn in view of the cancellation of the claims.

Response to Arguments

9. Claims 20, 29, 38-40, 55, 62-63, 68, 75-81 and 84-92 under 35 U.S.C. 103(a) as being unpatentable over Gillies et al (Human Antibodies and Hybridomas, 1(1):47-54, 1990, cited previously) as evidenced by the specification in view of Kashmiri et al (WO 00/26394, 5/11/00) and Anderson et al (U.S. Patent 6,348,581 B1, priority at least to 2/18/1998, cited previously) and Thorpe et al (U.S. Patent 6,342,219 B1, 4/28/1999, cited previously) is maintained.

The response filed 2/1/2006 summarizes the teachings of the cited references, reviews the rejection and cites various case law and MPEP 2142, which summarizes the three basic criteria to establish a *prima facie* case of obviousness. Applicant argues that the reliance on the instant specification as evidence that non-covalent association is an inherent property of CH2-domain-deleted antibodies in which the CH3 domain is fused directly to the hinge region, however, this reliance is misplaced and incorrect. Applicant states that extrinsic evidence may be offered to show that a reference anticipates a claimed invention and such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference and that it would be so recognized by persons of ordinary skill in the art, citing MPEP 2131.01. Applicant states that it is improper to use applicant's specification because the specification is not extrinsic evidence and one of ordinary skill in the art would not have recognized that non-covalent association is necessarily an inherent property of CH2 domain-deleted antibodies in which the CH3 domain is fused directly to the hinge region. This has been fully considered but is not found persuasive. The response does not challenge the motivation to combine the reference teachings, the reasonable expectation of success or that all the claim limitations are taught or suggested, the three criteria for establishing a *prima facie* obviousness as summarized in MPEP 2142 and pointed to by Applicant. The following is reiterated for Applicant's convenience. One of ordinary skill in the art would have been motivated and had a reasonable expectation of success to modify the CH2 domain deleted mouse antibody (B72.3) of Gillies et al in which the CH3 domain is fused directly to the hinge region with the humanized CC49

VH and VL sequences taught by Kashmiri et al to reduce the immunogenicity of the CH2 domain deleted antibody and enhance the therapeutic index of the CH2 domain deleted antibody as a targeting element for delivering various cytotoxic agents for human cancer therapy as taught by Anderson et al and Thorpe et al. Further, the teachings of Anderson et al and Thorpe et al evince that it was known and routine in the art at the time the instant invention was made to conjugate cytotoxic agents to an antibody for targeting and the art of Kashmiri et al teach that the humanized CC49 antibody comprising the heavy chain variable region of SEQ ID NO:7 and the light chain variable region of SEQ ID NO:9 retained specificity for the CC49 antigen. Thus, there was a reasonable expectation of success in making the above modifications. Therefore, the CH2 domain deleted CC49-specific antibody comprising the heavy and light chain variable regions sequences of SEQ ID Nos:7 and 9, respectively, wherein the CH3 domain is fused directly to the hinge region of the prior art is identical to the claimed CH2 domain deleted CC49-specific antibody and the CH2 domain deleted CC49-specific antibody of the prior art would necessarily non-covalently associate into a tetravalent dimeric CH2 domain deleted CC49-specific antibody. Applicant is reminded that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or

substantially identical processes, a prima facie case of obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). Therefore, even assuming that the specification is not "extrinsic" evidence, based on the discussion above, the combined teachings of the prior art would have directed one of ordinary skill in the art to the presently claimed tetravalent dimeric CH2 domain deleted CC49-specific antibody. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). See MPEP 2112.

Applicant's arguments regarding disclosed properties of the presently claimed dimeric antibody, which were not described or suggested by Gillies et al nor any of the other secondary references and would not have been expected at the time the invention was made have been fully considered but are not found persuasive for reasons set froth immediately above. Further, in response to applicant's arguments against the

references individually, one cannot show non-obviousness by attacking references individually where the rejection is based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, none of the cited references individually teach a tetravalent dimeric CH2 domain deleted CC49-specific antibody identical to that claimed and as such would have not been expected to have the claimed properties.

At page 13 of the response, Applicant argues that divalent anti-TAG-72 antibodies were an unexpected result that was not described or suggested by Gillies et al in combination with Kashmiri et al and Anderson et al and Thorpe et al and could not have been predicted by one of ordinary skill in the art. This has been fully considered but is not found persuasive because allegations of "unexpected results" must be supported by an appropriate affidavit or declaration. The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP 716.01(c).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejections is maintained.

Conclusion

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

SHEELA HUFF
PRIMARY EXAMINER